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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,579	09/05/2003	Kyusung Park	0942.5580002//BJD/JKM	6419

26111 7590 08/09/2006

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EXAMINER	
MUMMERT, STEPHANIE KANE	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/655,579	PARK ET AL.	
	Examiner	Art Unit	
	Stephanie K. Mummert, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *2 and 9-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1 and 3-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/9/04; 8/11/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1 and 3-8 in the reply filed on May 25, 2006 is acknowledged.

2. Claims 9-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 25, 2006.

3. Claims 1 and 3-8 are pending and will be examined.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on June 9, 2004 and August 11, 2004 were filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Specification

5. The use of the trademark AccuPrime™ has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 3-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Regarding claims 1 and 7, the inclusion of the term 'DNAP' is vague and indefinite. While it is presumed that this 'DNAP' term is intended to represent a DNA polymerase, the meaning of the term is unclear as currently recited. It is suggested that the term should be recited by its full name followed, if necessary, by the abbreviated term in parentheses.

9. Regarding claim 1, the inclusion of the terms 'RT' and 'SSB' are vague and indefinite. While it is presumed that 'RT' is intended to represent a reverse transcriptase and it is presumed that 'SSB' is intended to represent a single stranded binding protein, the exact meaning of the term is unclear as currently recited. It is suggested that the terms should be recited by their full names, followed, if necessary, by the abbreviated term(s) in parentheses.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1 and 3-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Du Breuil Lastrucci (US PgPub 2003/0228620; December 2003; 'Lastrucci' herein). Lastrucci discloses compositions for one-tube nested nucleic acid amplification reactions (Abstract).

With regard to claim 1, Lastrucci teaches a composition comprising:

(a) at least one anti-DNAP antibody (p. 14, paragraph 135, where the kit is contemplated as including one or more antibodies to the polymerase or polymerase subunits) and/or at least one anti-RT antibody; and

(b) at least one SSB (p. 14, paragraph 135, where the kit is contemplated as including one or more single strand binding proteins).

With regard to claim 3, Lastrucci teaches an embodiment of claim 1, further comprising one or more nucleic acid templates (p. 14, paragraph 135, where the kit is contemplated as including one or more templates).

With regard to claim 4, Lastrucci teaches an embodiment of claim 3, wherein at least one of said one or more templates is a cDNA (p. 14, paragraph 135, where the kit is contemplated as including one or more templates and paragraph 135, where a cDNA template is specifically contemplated; see also p. 12, paragraph 116-117, where it is noted that methods and compositions described may be used in conjunction with or include RT-PCR and cDNA).

With regard to claim 5, Lastrucci teaches an embodiment of claim 1, further comprising at least one primer (p. 14, paragraph 135, where the kit is contemplated as including one or more primers).

With regard to claim 6, Lastrucci teaches an embodiment of claim 1, further comprising one or more nucleotides (p. 14, paragraph 135, where the kit is contemplated as including one or more nucleotides - e.g., one or more deoxynucleotides and/or one or more exo-sample nucleotides).

With regard to claim 7, Lastrucci teaches an embodiment of claim 1, further comprising one or more DNAPs (p. 14, paragraph 135, where the kit is contemplated as including one or more thermostable DNA polymerases (either standard Taq, or recombinant Taq such as Platinum™ or ACCUPRIME Taq).

With regard to claim 8, Lastrucci teaches an embodiment of claim 1, further comprising one or more reverse transcriptases (p. 14, paragraph 135, where the kit is contemplated as including one or more templates and paragraph 135, where a cDNA template is specifically contemplated, generated by reverse transcription of the polyA tail of an mRNA target; see also p. 12, paragraph 116-117, where it is noted that methods and compositions described may be used in conjunction with or include RT-PCR and suitable reverse transcriptases are described).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1 and 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharkey et al. (Bio/Technology, 1994, vol. 12, p. 506-509; IDS reference) in view of Oshima

(Biotechniques, 1992, vol. 13, no. 2, p. 188) and further in view of Atwood et al. (US Patent 5,364,790; November 1994) and Nuovo et al. (US Patent 5,538,871; July 1996). Sharkey discloses compositions and methods for amplification using antibodies directed to the DNA polymerase from Thermus aquaticus (Abstract).

With regard to claim 1, Sharkey teaches a composition comprising:
(a) at least one anti-DNAP antibody and/or at least one anti-RT antibody (p. 509, 'antibody inhibition of DNA polymerase incorporation assay' heading, where the effect of antibodies on Taq polymerase activity was studied; 'use of antibodies to eliminate zero-cycle artifacts in PCR' heading, where PCR experiments were performed in which Taq polymerase was pre-incubated with anti-Taq polymerase antibodies; 'inactivation of antibody by heating' heading).

With regard to claim 3, Sharkey teaches an embodiment of claim 1, further comprising one or more nucleic acid templates (p. 509, 'use of antibodies to eliminate zero-cycle artifacts in PCR' heading, where PCR experiments were performed in which Taq polymerase was pre-incubated with anti-Taq polymerase antibodies and where PCR mixes were made with HIV target DNA).

With regard to claim 5, Sharkey teaches an embodiment of claim 1, further comprising at least one primer (p. 509, 'inactivation of antibody by heating' heading, where full PCR mixtures, including 1 μM each of primers SK38 and 5'biotinylated SK39, 1.5 mM each of dATP, dCTP, dGTP and dTTP, in addition to TP4 (an anti-Taq antibody) with no Taq polymerase, or TP4 with Taq polymerase).

With regard to claim 6, Sharkey teaches an embodiment of claim 1, further comprising one or more nucleotides (p. 509, 'inactivation of antibody by heating' heading, where full PCR

mixtures, including 1 μM each of primers SK38 and 5'biotinylated SK39, 1.5 mM each of dATP, dCTP, dGTP and dTTP, in addition to TP4 (an anti-Taq antibody) with no Taq polymerase, or TP4 with Taq polymerase).

With regard to claim 7, Sharkey teaches an embodiment of claim 1, further comprising one or more DNAPs (p. 509, 'inactivation of antibody by heating' heading, where full PCR mixtures, including 1 μM each of primers SK38 and 5'biotinylated SK39, 1.5 mM each of dATP, dCTP, dGTP and dTTP, in addition to TP4 (an anti-Taq antibody) with no Taq polymerase, or TP4 with Taq polymerase).

Regarding claim 1, Sharkey does not disclose the inclusion of a single stranded binding protein or SSB in the composition. Oshima discloses methods and compositions directed to the increase of amplification efficiency and specificity of an amplification reaction (p. 188, col. 2).

Regarding claim 1, Oshima teaches a composition comprising at least one SSB (p. 188, col. 2, where amplification reactions were supplemented with 1 μg SSB, which resulted in the highest yield of the expected product).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the compositions and teachings of Oshima to the compositions and teachings of Sharkey to arrive at the claimed invention with a reasonable expectation for success. As taught by Oshima, "E. coli single-stranded DNA binding protein (SSB) was found to be extremely useful in obtaining full-length amplification products of some gene fragments (p. 188, col. 1)". Oshima also notes that "Supplementation of a 25 μl PCR containing 100 ng of mouse genomic DNA with 1 μg of SSB resulted in the highest yield of the expected product (lane 3)" (p. 188, col. 2). Furthermore, Atwood directly states, "published

work on in situ PCR has shown that to preserve highly specific amplification it is often important to assemble the reaction so as to achieve a 'hot start' or chemical equivalent" (col. 3, lines 16-23). Atwood also teaches that "one way a 'chemical hot start' in a PCR can be achieved is by including, in the reagent, a heat-labile component such as single strand binding protein (SSB) which prevents any extension by the polymerase enzyme until the reaction mixture has been heated in the first PCR cycle to a temperature high enough to prevent non-specific hybridization and also to destroy the heat-labile SSB component" (col. 3, lines 34-41). Finally, Atwood notes "a still further way of implementing a chemical hot start is to combine the Taq polymerase enzyme with a Taq antibody before adding it to the reagent" (col. 3, lines 47-49). While Atwood does not explicitly suggest incorporating more than one type of 'chemical hot start' in a single amplification reaction or composition, there is a clearly stated connection between these different types of amplification additives, designed to avoid non-specific amplification. A related disclosure by Nuovo states "although the three basic tactics of PCR specificity enhancement (HotStart™ methods, amplified DNA restriction, and SSB addition to the reaction mixture) each can serve alone to improve specific amplification, combinations of the three approaches may have special benefits" (col. 4, lines 54-58). Nuovo in view of the teachings of Atwood, Oshima and Sharkey, provides a direct motivation to combine more than one type of PCR specificity enhancements to achieve "special benefits" to the amplification process. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the single stranded binding protein taught by Oshima to the amplification composition comprising anti-Taq polymerase antibodies of Sharkey to achieve improved amplification specificity and enhancement.

14. Claims 4 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharkey et al. (Bio/Technology, 1994, vol. 12, p. 506-509) in view of Oshima (Biotechniques, 1992, vol. 13, no. 2, p. 188) and further in view of Atwood et al. (US Patent 5,364,790; November 1994) and Nuovo et al. (US Patent 5,538,871; July 1996) as applied to claims 1 and 3-7 above, and further in view of Spagnuolo-Weaver et al. (Veterinary Microbiology, 2000, vol. 76, p. 15-23). Sharkey discloses compositions and methods for amplification using antibodies directed to the DNA polymerase from Thermus aquaticus (Abstract).

Sharkey in view of Oshima and further in view of Atwood teaches all of the limitations of claims 1 and 3-7 as recited in the 103 rejection above. However, neither Sharkey, Oshima or Atwood explicitly disclose the inclusion of anti-DNAP or SSB in reactions or compositions which incorporate cDNA and/or reverse transcriptase.

With regard to claim 4, Spagnuolo-Weaver teaches an embodiment of claim 3, wherein at least one of said one or more templates is a cDNA (p. 17, 'Total RNA extraction and cDNA preparation' heading, where total RNA was converted to cDNA and the cDNA was used in an amplification reaction, see 'PCR' heading).

With regard to claim 8, Spagnuolo-Weaver teaches an embodiment of claim 1, further comprising one or more reverse transcriptases (p. 17, 'Total RNA extraction and cDNA preparation' heading, where total RNA was converted to cDNA using MMLV reverse transcriptase).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of Spagnuolo-Weaver to the composition of

Sharkey and Oshima to arrive at the claimed invention with a reasonable expectation for success. As taught by Spagnuolo-Weaver, "a number of reverse transcriptase-polymerase chain reaction (RT-PCR) assays have been developed for the detection of PRRS viral nucleic acid in serum and other diagnostic samples" (p. 16, 'introduction' heading). Spagnuolo-Weaver discloses a method for detection of PRRS viral RNA in serum samples using a fluorimeter-based PCR (p. 16) and also notes that "the PCR assays were carried out in a fluorimeter-based thermocycler... using chemical hot start-PCR. For this, an anti-Taq polymerase antibody (Platinum Anti-Taq Antibody, Life Technology) was mixed in the appropriate buffer containing the Taq polymerase (1U Ab/1U enzyme), incubated at room temperature for 20 minutes and immediately used" (p. 18, top paragraph). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the cDNA templates taught by Spagnuolo-Weaver to the composition of Sharkey and Oshima to achieve enhanced amplification results.

Request for Information under 37 CFR § 1.105

Applicant and the assignee of this application are required under 37 CFR § 1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application.

An issue of public use or on sale activity has been raised in this application. In order for the examiner to properly consider patentability of the claimed invention under 35 U.S.C. § 102(b), additional information regarding this issue is required as follows.

Applicant is reminded that failure to fully reply to this requirement for information will result in a holding of abandonment.

This request is being made for the following reasons:

A document substantially describing the claimed composition was obtained from the Invitrogen website, with a printing/publication date of 2001 (see attached document, "AccuPrime™ Taq DNA polymerase"; 'Document 1' herein). The document includes a description of "AccuPrime™ Taq DNA polymerase" and goes on to describe the inclusion of the AccuPrime™ polymerase as part of a hot-start PCR reaction, including an anti-Taq antibody, and an AccuPrime™ accessory protein, which is being interpreted as being a single-stranded DNA binding protein. The inclusion of these components into a composition for amplification of a general template in a PCR reaction is described throughout the document and is also depicted schematically at Figure 1. However, because the authorship and specific publication date are not provided, it is not possible to determine the potential for this document to be applied as prior art.

A composition, SuperMix II, is also included as part of this document and is described in greater detail in the product literature (see "AccuPrime™ SuperMix II" brochure attached, publication date 1/24/02, 'Document 2' herein). SuperMix II is disclosed in the instant application as including anti-Taq DNA polymerase antibodies, a thermostable AccuPrime™ protein (i.e., *Methanococcus jannachii* SSB), magnesium, deoxyribonucleotide tripophosphates, and recombinant Taq DNA polymerase at concentrations sufficient to allow amplification during PCR (Example 2, p. 12, paragraph 162 of PgPub). However, because the authorship/inventorship is not provided for this document, it is not possible to determine the potential for this document to be applied as prior art.

Applicants and the Assignee of this application are required under 37 CFR § 1.105 to provide the following information that the examiner has determined is reasonably necessary to

the examination of this application.

The information is required to determine whether the composition was available to the public, accessibility of any foreign sales and the reproducibility of any composition that were sold to the public, more than one year prior to the effective filing date of this application.

In response to this requirement please provide:

a) information available regarding the first sale or other public distribution of the claimed composition anywhere in the United States more than one year prior to the effective filing date of this instant application, including date(s) and location of any sale or other public distribution including any public information available regarding sales, offers for sale, or public distributions of the claimed composition that occurred more than one year prior to the effective filing date of this application, including information pertaining to whether this was an obscure, solitary occurrence that would go unnoticed by those skilled in the art;

b) evidence of any restrictions placed upon the further sale/resale, or other distribution of the composition;

c) information about who was distributing the composition in the United States that occurred more than one year prior to the filing date of the instant application. Please also provide information about who was distributing the composition outside the United States that occurred more than one year prior to the filing date of the instant application;

d) information about the relationship between the distributor(s) and the inventor and/or the assignee.

e) information regarding the earliest publication date and authorship for documents disclosing the composition, including informational brochures (e.g., Document 1), product

literature (e.g., Document 2) and other technical support documents which were available to the public prior to the earliest effective filing date of the instant application.

If Applicant views any or all of the above requested information as a Trade Secret, then Applicant should follow the guidance of MPEP § 724.02 when submitting the requested information.

The fee and certification requirements of 37 CFR § 1.97 are waived for those documents submitted in reply to this requirement. This waiver extends only to those documents within the scope of this requirement under 37 CFR § 1.105 that are included in the applicant's first complete communication responding to this requirement. Any supplemental replies subsequent to the first communication responding to this requirement and any information disclosures beyond the scope of this requirement under 37 CFR § 1.105 are subject to the fee and certification requirements of 37 CFR § 1.97.

The applicant is reminded that the reply to this requirement must be made with candor and good faith under 37 CFR § 1.56. Where the applicant does not have or cannot readily obtain an item of required information, a statement that the item is unknown or cannot be readily obtained may be accepted as a complete reply to the requirement for that item.

This requirement is an attachment of the enclosed Office action. A complete reply to the enclosed Office action must include a complete reply to this requirement. The time period for reply to this requirement coincides with the time period for reply to the enclosed Office action.

Conclusion

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Sorge et al. (US PgPub 2004/0081965; April 2004) discloses a composition which includes a modified polymerase blended with additives like antibodies and single stranded DNA binding proteins (paragraph 108).

This Office action has an attached requirement for information under 37 CFR 1.105. A complete reply to this Office action must include a complete reply to the attached requirement for information. The time period for reply to the attached requirement coincides with the time period for reply to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stephanie K. Mummert

Stephanie K Mummert, Ph.D.
Examiner
Art Unit 1637

SKM

Kenneth R. Horlick

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

8/7/06